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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,985	12/19/2001	Carine Capiau	B45182	2966

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EXAMINER	
FORD, VANESSA L	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,985	CAPIAU ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-9,11,12,14 and 15* is/are pending in the application.

4a) Of the above claim(s) *12,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. This Office Action is responsive to Applicant's amendment and response filed August 2, 2004. Claims 1-4, 6, 9 and 11 have been amended. Claims 5, 10 and 13 have been cancelled.

2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

3. The rejection under 35 U.S.C. 103(a) is maintained for claims 1-4, 6-9 and 11 for the reasons set forth on pages 2-5, paragraph 4 of the previous Office Action.

The rejection was on the grounds that Kuo et al teach a composition comprising immunogenic polysaccharide-protein conjugates and pneumolysin protein of *Streptococcus pneumoniae* (see the Abstract). Kuo et al teach that capsular polysaccharides of various pneumococcal types (for example, types 6B, 14C, 18C and 20) are used in their inventions (column 5, lines 17-28 and column 6, Example 1). Kuo et al teach that the composition may be added to immunologically acceptable diluents or carriers in the conventional manner to prepare injectable liquid solutions or suspensions (column 5, lines 45-47). Kuo et al teach that the conjugates of the invention may be bound to aluminum hydroxide, aluminum phosphate (alum), QS-21, monophosphoryl lipid A and deacylated monophosphoryl lipid A (which induce strong TH1 responses) (column 5 lines 47-51). It is well known in the art to add protein carriers such as keyhole limpet haemocyanin (KLH), diphtheria toxoid, tetanus toxoid and protein derivative of Tuberculin (PPD) to antigens to enhance the immunogenicity of the antigen this is evidenced by *(U.S. Patent No. 6,419,932, U.S. Patent No. 4, 761, 283, U.S. Patent No. 6,224,880 and U.S. Patent No. 5,360,897).*

Kuo et al do not teach choline binding proteins.

Masure et al teach a vaccine comprising choline binding proteins (CBPs) (column 6, lines 65-67 and column 7, lines 1-8). Masure et al teach vaccines comprising CBP antigen or antigenic derivative or fragment thereof or a CBP nucleic acid vaccine that can be administered via any parenteral route including but not limited to intramuscular, intraperitoneal, intravenous and the like (column 24, lines 57-61). Masure et al suggest that criteria to consider in selecting a

preferred CBP as a vaccine candidate includes testing CBP defective mutants for attenuation of virulence in animal models for bacteremia or colonization efficacy alone or in combination or coupled to a capsular polysaccharide (column 14, lines 41-46). Masure et al teach that the vaccines of the invention can be comprises an active material such as a diluent (i.e. carrier or vehicle) (column 29, lines 14-20). Masure et al teach that CBP or fragment thereof can be conjugated to an immunogenic carrier, e.g. bovine serum albumin (BSA) or keyhole limpet hemocyanin (KLH) (column 22, lines 5-8).

It would be *prima facie* obvious at the time the invention was made to add the CBP vaccines of Masure et al to the pneumococcal polysaccharide recombinant pneumolysin conjugate vaccines as taught by Kuo et al because Masure et al teach that one may administer the CBP vaccines in conjunction with one or more pharmaceutical compositions used for treating bacterial infection, including but no limited to antibiotics, soluble carbohydrate inhibitors of bacterial adhesion, other small molecule inhibitors of bacterial adhesion, inhibitors of bacterial metabolism, transport or transformation, stimulators of bacterial lysis or antibacterial antibodies or vaccines directed at other bacterial antigens (column 30, lines 34-42). It would be expected barring evidence to the contrary, that the addition of the CBP vaccines of Masure et al to the pneumococcal polysaccharide recombinant pneumolysin conjugate vaccines as taught by Kuo et al would be effective in treating *Streptococcus pneumoniae* infections.

Applicant urges that to establish a *prima facie* case of obviousness there must a suggestion or incentive that would motivate one skilled in the art to modify a reference or combination of references. Applicant urges that in all the examples of specification (4B, 4C and 5) the *Streptococcus pneumoniae* antigen is the second component and is used in unconjugated form. Applicant urges that there is no mention of any need to further supplement the vaccine of Kuo et al to improve its efficacy against pneumococcal disease. Applicant urges that there is no clear direction to use a Th1 adjuvant in the composition. Applicant urges that the skilled person would have to be motivated to select antibacterial vaccines, choose *Streptococcus pneumoniae* antigens from all antibacterial vaccines, decide to add pneumococcal polysaccharide conjugate antigens and be

motivated to select a Th1 adjuvant. Applicant urges that a person skilled in the art would not have carried out these quantum leaps with any reasonable expectation the advantages obtained as set out in the present invention and to suggest otherwise would involve hindsight analysis of the prior art using the teaching of the present invention which of course is an impermissible approach to the analysis of obviousness. Applicant urges that neither Kuo et al nor Masure et al discuss the advantages of combining pneumococcal polysaccharide conjugates with CbpA and Th1 adjuvant to achieve the claimed invention. Applicant urges that there is no motivation anywhere to combine these antigens into a composition.

Applicant's arguments filed August 2, 2004 have been fully considered but they are not persuasive. It is the position of the Examiner that the claims recite "comprising" which is open claim language. Therefore, the claimed elements may be comprised in the claimed composition along with any other elements. In other words, the claims are no so limited to the *Streptococcus pneumoniae*-protein conjugates, unconjugated *Streptococcus pneumoniae* antigen and an adjuvant which is a preferential inducer of a TH1 response. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)

and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill in the art would be motivated to use the *Streptococcus pneumoniae* polysaccharide-protein conjugate and an adjuvant which is a preferential inducer of a TH1 response of Kuo et al in combination with the *Streptococcus pneumoniae* protein antigen (choline binding proteins) of Masure et al because both have been shown to be protective against *Streptococcus pneumoniae* infections. It should be noted that Masure et al teach that the choline binding proteins or fragments thereof mediated adhesion. One of ordinary skill in the art would be motivated to add choline binding proteins or fragments thereof to other vaccine components to prevent bacteria from adhering to the cell surface, thereby preventing infection. If a bacterium cannot adhere to the cell surface then infection is minimized. One of ordinary skill in the art would have been motivated to use a TH1 adjuvant because these adjuvants have been shown to be effective as adjuvants in *Streptococcus* vaccine compositions. The vaccine composition as taught by Kuo et al are used to target infections caused by *Streptococcus pneumoniae*. Therefore, a vaccine composition comprising the choline binding proteins or fragments thereof as taught by Masure et al and the polysaccharide-protein conjugates and adjuvants as taught by Kuo et al can be use as multi-component, multi-purpose vaccines for protection against pneumococcal infections.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction

based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

New Grounds of Rejection Necessitated by Amendment

Claim Objection

4. Claim 11 is objected to because if depends from"... any one of claims 1-9". It should be noted that claim 5 has been cancelled. Therefore, the claim depends from a cancelled claim because claim 5 is included in the phrase "any one of 1-9". Correct is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Newly amended claims 1-4, 6, 9 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. *This is a new matter rejection.* The amendment filed August 3, 2004 introduced new matter into the claims.

Claims 1-4, 6, 9 and 11 recite "an immunogenic composition comprising at least one *Streptococcus pneumoniae* polysaccharide-protein conjugated, with at least one unconjugated *Streptococcus pneumoniae* protein and an adjuvant which is a preferential inducer of a TH1 response.

Newly submitted claims introduce new matter in the claims because "the phrase "unconjugated *Streptococcus pneumoniae* protein" which is not disclosed, taught or supported in the instant specification. Applicant has failed to direct the Examiner as to where in the instant specification the support for this amendment is specifically shown or implied. The Examiner has reviewed the instant specification and has failed to find the support for the amendment. Removal of the phrase "unconjugated *Streptococcus pneumoniae* protein" from the claims is requested.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory

period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272–0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
October 20, 2004

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